510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number: K031579

B. Analyte: lithium

C. Type of Test: quantitative fluorescence assay

D. Applicant: Akers Laboratories Inc.

E. Proprietary and Established Names: InstaRead™ Lithium System

F. Regulatory Information:

1. Regulation section: 21CFR862.3560, Lithium Test System

2. Classification: Class II

3. Product Code: JIH

4. Panel: Toxicology (91)

G. Intended Use:

1. Indication(s) for use: The InstaRead™ Lithium System is intended to measure lithium blood levels. Measurements of lithium are used to aid in the management of individuals taking lithium for the treatment of mental disturbances, such as manic-depressive illness (bipolar disorder). The test is targeted for physician's office use and may be used with whole blood, serum or EDTA-plasma.

2. Special condition for use statement(s): Results should be interpreted in conjunction with clinical findings and levels above1.5 mEq/L should be corroborated.

3. Special instrument Requirements:

H. Device Description:

The test system is a tabletop system and includes a blood separator (cassettes), reagent-filled cuvettes, calibrator and test reader (spectrophotometer). It also includes fingerstick blood sampling supplies.

I. Substantial Equivalence Information:

1. Predicate device name(s): Johnson and Johnson Clinical Diagnostics Vitros Lithium System.

2. Predicate K number(s): K934106

3. Comparison with predicate: Both devices measure lithium as an aid management of patients taking lithium. The predicate device uses serum or plasma samples; InstaRead™ can also accept whole blood as a sample type since it includes a blood cell separator as part of the system. InstaRead™ is indicated for use in physician's offices; the predicate is intended for laboratory use. Both devices use colorimetric spectrophotometry, although the reagents differ. The upper range of linearity for this device is to 2.5 mEq/L; the predicate device is linear to 4.0 mEq/L.

J. Standard/Guidance Document Referenced (if applicable):

K. Test Principle: The device includes a blood cell separator component, reagents for lithium measurement and a photometric reader. The whole blood separator includes a membrane which is designed to capture blood cells by lectin binding as well as deliver a specific sample volume to be added to the lithium reagent. The reagent contains a porphyrin which, when bound to lithium, causes an increase in light absorbance at 505 nm. Absorbance is measured and displayed by the photometric reader.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-day precision of spiked serum samples was evaluated at concentrations (determined by a reference laboratory method) spanning the range of 0-1.9 mEq/L . Seven determinations were made for each sample within one day. Results are tabulated below:

Target concentration (mEq/L)	Range observed(mEq/L)	Standard deviation (mEq/L)
0.0	0.0	0.0
0.12	0.1-0.2	0.04
0.24	0.2-0.3	0.05
0.30	0.3	0.00
0.47	0.5-0.6	0.05
0.60	0.5-0.6	0.05
0.84	0.8-0.9	0.04
0.95	0.9	0.00
1.20	1.1-1.3	0.08
1.55	1.4-1.5	0.04
1.90	1.7-1.9	0.08

Precision over 5 days was evaluated using clinical serum samples at concentrations of 0.51 and 1.23 mEq/L, as determined by a reference laboratory. Each sample was analyzed by the ™ System10 times per day for 5 days (total n per sample=50). Results are tabulated below:

Target level (mEq/L)	Mean concentrations observed (range over 5 days)	Standard deviations (range over 5 days)
0.51	0.5-0.6	0.06-0.07
1.23	1.3-1.4	0.05-0.08

Precision with EDTA plasma samples was evaluated over 3 days, using samples at concentrations of 0.3 and 0.7 mEq/L, as quantitated by a reference laboratory. Each sample was analyzed by the Instaread™ 10 times per day for 3 days (total n per sample = 30). Results are tabulated below:

Target level (mEq/L)	Mean concentrations observed (range over 3 days)	Standard deviations (range over 3 days)
0.3	0.3-0.4	0.05-0.11
0.7	0.8-0.9	0.04-0.06

Within-run precision for whole blood samples was evaluated using two spiked EDTA whole blood samples. Two operators and two readers were incorporated in this evaluation. Results shown below were determined from 40 replicates for each level (20 replicates per reader). There was no observed effect of Operator or Instrument on precision. (These results are shown as 2 significant figures, however the marketed device reads to 1 significant figure.)

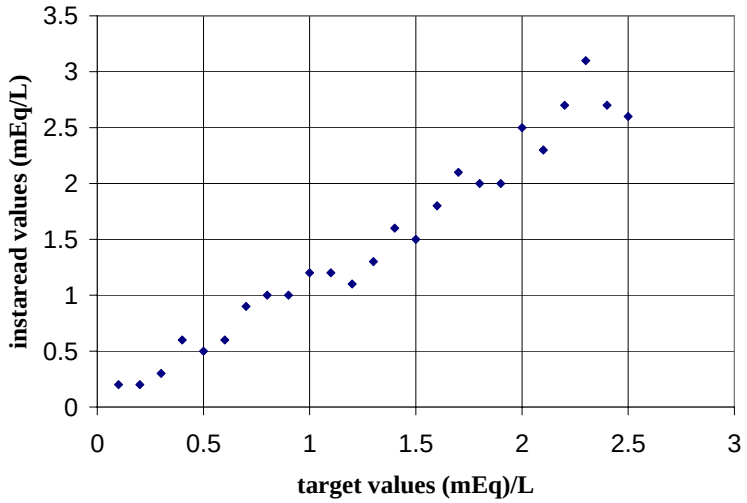
Target Level (mEq/l)/Operator/Reader	Mean	SD	%CV
0.5/Operator 1/Both readers	0.41	0.05	11.8
1.2/Operator 1/Both readers	1.02	0.08	7.4
0.5/Operator 2/Both readers	0.38	0.05	13.7
1.2/Operator 2/Both readers	1.03	0.09	8.9

Precision was also assessed over 20 days for 2 levels of lithium controls. The following results were obtained based on the average of all values over the 20 days:

Mean value	SD	%CV
0.49	0.04	8.1
1.26	0.06	4.4

b. *Linearity/assay reportable range:*

The instrument reports values between 0-2.5 mEq/L lithium. Linearity was evaluated with samples prepared by diluting a concentrated LiCl solution into serum and EDTA-plasma samples. Twenty five prepared serum samples and 11 prepared plasma sample in the range between 0-2.5 mEq/L were evaluated. Results with serum are summarized below. Results with plasma show comparable linearity.



c. Traceability (controls, calibrators, or method):
Calibrators are prepared from commercially available material that is analyzed and assigned by atomic absorption spectroscopy. Calibrators are further evaluated using assay reagents on an automated analyzer. Acceptance criteria are that recoveries of test standards and control standards (previously approved fill) must agree within 5%.
Observed recoveries for accelerated stability testing (45 degrees C, 5.5 days, 60 degrees C for 28 hours) were between 99-102%. Acceptance criteria are that recoveries should be within 10% of "fresh" sample results.
Real-time stability studies are ongoing.
External controls are available commercially.

d. *Detection limit:* Whole blood free of lithium was assayed 20 times within one day. Results ranged from 0 to 0.16 mEq/L (which will read as 0.2 on the marketed device.) The mean was .054 and 2SD = 0.082. Comparable results were obtained in testing with serum.

e. *Analytical specificity:* To evaluate potential interference from endogenous compounds, the following compounds were spiked into a commercially available serum control containing approximately 1 mEq/L lithium:

conjugated bilirubin up to 769 uMol/L,
triglycerides up to 22.6 mMol/L,
hemoglobin up to 1000 mg/dL.

Less than 10% deviation was observed for bilirubin and triglycerides.
Less than 5% deviation was observed from hemoglobin up to 1000 mg/dL.
To evaluate potential interference from endogenous compounds, the following compounds were spiked into a commercially available serum control containing approximately 1 mEq/L lithium:

N-acetylcysteine at 90 mg/dL,
Carbamazepine at 12 ug/ml,
Procainamide at 8 ug/ml,
Quinidine at 6 ug/ml,
Valproic Acid at 100 ug/ml.

Less than 10% assay bias was observed for samples containing these drugs.

To evaluate potential assay interference by other ions, the following were tested with assay reagents in solutions containing 1 mEq/L lithium:

Sodium up to 200 mmol/L
Potassium up to 8 mMol.L
Calcium up to 4 mMol/L
Magnesium up to 2 mMol/L
Iron up to 200 uMol/L
Zinc up to 250 uMol/L
Copper up to 250 uMol/L

Less than 5% deviation from expected results was observed.

f. Assay cut-off: Not applicable. The device is quantitative.

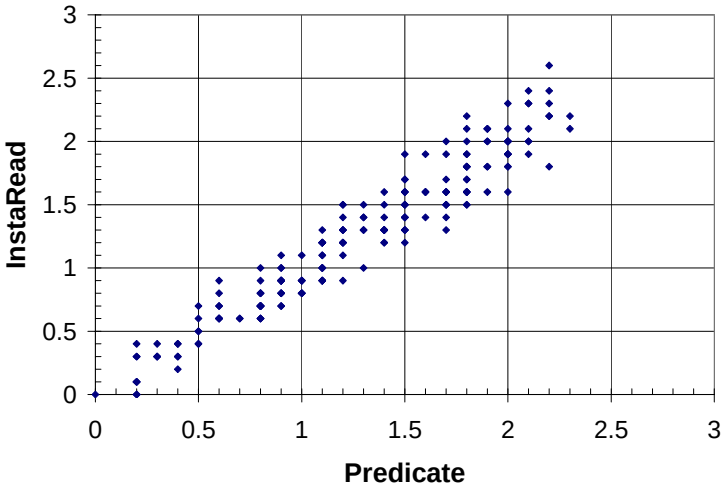
2. Comparison studies:

a. Method comparison with predicate device:

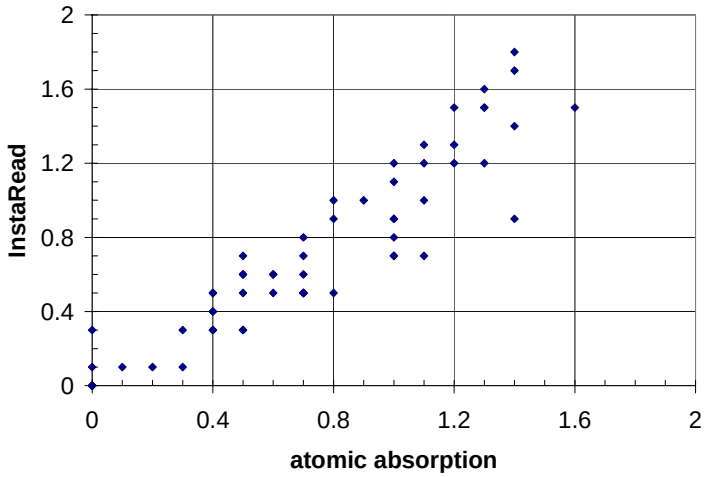
Three types of samples were evaluated in terms of comparison to previously cleared devices. (1) One hundred serum samples were evaluated at each of two central laboratories and compared to results obtained with predicate devices. (2) Twenty nine spiked whole blood samples were evaluated at a physician's office and compared to the predicate device. (Samples were processed to plasma before they were evaluated with the predicate device). (3) Clinical fingerstick blood samples were evaluated at one physicians office in two separate studies. Subjects were consenting adults currently taking lithium under care of the physician at the site; there were no other specific inclusion/exclusion criteria. At that site, venous whole blood and fingerstick samples were collected from each patient. Fingerstick samples were measured by the Instaread™ Lithium Test and venous whole blood samples were processed to serum and evaluated at a reference laboratory by a predicate device. All samples were masked. Summaries of results of all the studies are summarized below:

Sample type	Serum	Serum	Fingerstick	Fingerstick	Spiked whole blood
Site type	Central Lab	Central Lab	Physician's office	Physician's office	Physician's office
Sample #	100	100	40	20	29
Range (mEq/L)	0-2.3	0-2.5	0-1.6	0-1.8	0.1-2.4
Comparator	Vitros	Vitros	AA (matched serum)	AA (matched serum)	Vitros (matched plasma)
Slope *(95%CI)*	0.97	1.025	0.85 *(0.74-0.96)*	1.2 *(1.13-1.26)*	0.83 *(0.77-0.90)*
Int *(95%CI)*	0.03 *(-0.04- 0.1)*	-0.07 *(-0.15-0.02)*	0.02 *(-0.07-0.11)*	0 *(-0.06-0.06)*	0.05 *(-0.03-0.13)*
R	0.97	0.96	0.93	0.99	0.98
$Sy\|x$	0.14	0.17	0.14	0.06	0.10
Average bias relative to predicate	-0.01	-0.03	-0.09	0.16	-.13

The graph below illustrates combined data for the two serum studies:



The graph below illustrates combined data for the two physician office fingerstick studies:



3. Clinical studies:
   a. *Clinical sensitivity:* Not applicable. Not typically provided for this device type.

   b. *Clinical specificity:* Not applicable. Not typically provided for this device type.

   c. *Other clinical supportive data (when a and b are not applicable):*

4. Clinical cut-off: Not applicable. The device is for quantitative measurements.

5. Expected values/Reference range: The package insert recommends that clinicians should make their own assessments regarding patient status and lithium concentrations. Appropriate levels may vary among patients and may depend slightly on the specific assay used. Lithium values should be interpreted in conjunction with other clinical findings and values above 1.5 mEq/L should be corroborated. The package insert also cites the following. Mild to moderate adverse events may occur at concentrations between 1.5-2.5 mEq/L and moderate to severe reactions may occur at concentrations above 2.0 mEq/L, based on measurements 8-12 hrs post-dose.

M. System Descriptions:

1. Modes of Operation:
   The reader measures absorbance of a solution containing the separated sample and reagents.

2. Software:
   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:
   Yes ___X___ or No _____

3. Sample Identification:
   None.

4. Specimen Sampling and Handling:
   Fingerstick samples are applied to the whole blood separator. Specific volumes of sample (serum or plasma) are then collected in a pipette by the separator unit and added manually to the reagent.

5. Assay Types:
   Chemical binding, Quantitative

6. Reaction Types:
   Absorbance

7. Calibration: Calibration is performed by the instrument using an external calibrator provided to the user. Calibration information is stored in the instrument.

8. Quality Control: External quality control materials are commercially available.

N. Other Supportive Instrument Performance Characteristics Data Not Covered In The "L. Performance Characteristics" Section Of The SE Determination Decision Summary. The collection device was previously cleared under K030815.

O. Conclusion: I recommend that the Akers InstaRead™ Lithium System is substantially equivalent to the predicate device.